REMARKS

Claims 22 and 27–29 are pending and under consideration in the instant application. With this amendment, Applicant amends claims 22, 27, and 29, and introduces new claims 140–144 depending therefrom.

Amendments to the Claims

Applicant respectfully requests consideration of the amendments to claims 22 and 27–29 presented herein.

Applicant amends the preamble to claim 22 to recite a method of constructing a representation of a set of molecules stored in a computer database for facilitating searching thereof. Applicant then introduces an additional and final step to claim 22. Support for these amendments can be found in the specification as filed at, for example, page 25, line 27 to page 26, line 2.

Applicant also amends claim 22 in several ways for purpose of clarification. In particular, Applicant replaces "a distance geometry technique" with "distance geometry". Applicant inserts the word "specifying" for purposes of clarification, and amends the "determining" step of claim 22 to more particularly recite that which is considered to be the invention, support for which can be found at page 40, lines 5–10, and page 45.

Applicant amends claim 27 to ensure consistency with the language of claim 22.

Applicant amends claim 29 to recite a computer database used by a pharmaceutical company, an amendment which finds support in Applicant's specification at, *e.g.*, page 2, line 8.

Applicant also introduces new claims 140–144. Claim 140 finds support in the specification as filed at page 50, line 5 to page 51, line 11.

Claim 141 finds support at page 45, lines 27–28.

Claim 142 finds support at page 11, line 31, to page 12, line 1.

Claim 143 is supported at page 39, line 25 to page 40, line 2.

Finally, claim 144 is supported by the specification as filed at page 12, lines 1–4.

No new matter is believed introduced by these amendments, and entry thereof is respectfully requested.

Telephonic Interview

Applicant's representatives, Francis E. Morris, and Richard G. A. Bone, thank Primary Examiner Marschel, and Supervisory Examiner Woodward for courtesies extended

during the telephonic interview of August 20, 2004, and submit herein in connection with arguments presented, a recordation of the substance of the interview.

REJECTIONS OF THE CLAIMS

Rejections under 35 U.S.C. § 112 (¶ 1)

Scope of Lack of Enablement, and Lack of Enablement

The Examiner has rejected claims 22 and 27 – 29 under 35 U.S.C. § 112 (first paragraph) for alleged lack of enablement, and for alleged lack of enablement commensurate in scope with the claims. In connection with both rejections, the Examiner emphasized that he perceived a lack of evidence that distance geometry is widely practiced in the art, beyond the citation in Applicant's specification to a review article by Blaney *et al.* ("Blaney").

Specifically, the Examiner notes "that only one alleged distance geometry calculation has been pointed to or argued by applicant as set forth in Blaney *et al.*" and therefore that Blaney allegedly does not enable the full scope of the claim. The Examiner additionally alleges that "Blaney et al. ... is utilized in the instant disclosure as incorporating by reference essential subject matter". In particular, the Examiner considers that "only one methodology for constructing matrix G from D has been argued as being set forth in Blaney et al. ..., albeit with allegations of others [which] have not been supported by any documentary evidence or other facts."

Applicant respectfully traverses these rejections on the grounds that distance geometry has a wider purview in the art than has hitherto been supported by a reference to Blaney alone, and supports this premise with a number of literature publications, excerpts from text books, and descriptions of published computer programs for carrying out distance geometry calculations.

In a telephonic interview with Applicant's representatives, August 20, 2004, the Examiner reiterated his position that the instant claims are enabled only for distance geometry as described in Blaney and that the alleged lack of enablement could be cured by amending the specification to incorporate the relevant portions of Blaney therein. However, in response to Applicant's representatives' arguments that Blaney is not essential matter because distance geometry is well known in the art, the Examiner volunteered that he would consider factual support for such a premise, such as "half a dozen articles that refer to distance geometry."

Accordingly, Applicant submits some 25 references that describe the theory, practice, and application of distance geometry in a variety of technical arts prior to the filing date of the instant application. Several of these articles are cited to in the review article by Blaney, but many hail from other technical fields. All of these references are cited on a PTO-1449 form ("List of References Cited") in connection with an information disclosure statement filed herewith, and copies are provided.

In brief, the articles are categorized as follows.

A.) Published text books that describe the theory and various applications of distance geometry date back to 1953, examples of which are:

1) Blumenthal, *Theory and Applications of Distance Geometry*, Chelsea Publishing Company, (2nd Ed., 1970 – reprint of 1st Ed., 1953). [Title page, publisher information, and table of contents only.]

2) Crippen, *Distance Geometry and Conformational Calculations*, Research Studies Press Ltd., (1981).

3) Crippen and Havel, *Distance Geometry and Molecular Conformation*, Research Studies Press Ltd., (1988). [Title page, publisher information, and table of contents only.]

4) Leach, *Molecular Modelling*, Addison Wesley Longman Ltd., (1996). See, for example, excerpt at pages 426 – 434. [Title page, publisher information, table of contents, and excerpted pages only.]

B.) Journal articles that describe the theory and application of distance geometry in computational chemistry include:

5) Crippen and Havel, "Stable Calculation of Coordinates from Distance Information", *Acta Cryst.*, Vol. A34, 282-284, (1978).

6) Wenger and Smith, "Deriving Three-Dimensional Representations of Molecular Structure from Connection Tables Augmented with Configuration Designation Using Distance Geometry" *J. Chem. Inf. Comput. Sci.*, Vol. 22, 29-34, (1982).

7) Havel, *et al.*, "The Theory and Practice of Distance Geometry", *Bulletin of Mathematical Biology*, Vol. 45, No. 5, 665-720, (1983).

8) Kuszewski, *et al.*, "Sampling and efficiency of metric matrix distance geometry: A novel partial metrization algorithm", *Journal of Biomolecular NMR*, Vol. 2, 33-56, (1992).

C.) Journal articles that describe application of distance geometry to problems in conformational analysis of organic molecules include:

9) Weiner, *et al.*, "A Distance Geometry Study of Ring Systems: Application to Cyclooctane , 18-Crown-6, Cyclododecane and Androstanedione", *Tetrahedron*, Vol. 39, No. 7, 1113-1121, (1983).

10) Crippen, *et al.*, "Use of Augmented Lagrangians in the Calculation of Molecular Conformations by Distance Geometry", *J. Chem. Inf. Comput. Sci.*, Vol. 28, 125-128, (1988).

11) Peishoff, *et al.*, "Application of the Distance Geometry Algorithm to Cyclic Oligopeptide Conformation Searches", *Biopolymers*, Vol. 30, 45-56, (1990).

12) Wertz, *et al.*, "A Comparison of Distance Geometry and Molecular Dynamics Simulation Techniques for Conformational Analysis of ß-Cyclodextrin", *Journal of Computational Chemistry*, Vol. 13, No. 1, 41-56, (1992).

13) Spellmeyer, *et al.*, "Conformational Analysis Using Distance Geometry Methods", *Journal of Molecular Graphics and Modelling*, Vol. 15, 18-36, (1997).

D.) Journal articles that describe application of distance geometry to problems in protein structure determination by NMR include:

14) Cohen and Sternberg, "On the Use of Chemically Derived Distance Constraints in the Prediction of Protein Structure with Myoglobin as an Example", *J. Mol. Biol.*, Vol. 137, 9-22, (1980).

15) Havel and Wüthrich, "A Distance Geometry Program for Determining the Structures of Small Proteins and Other Macromolecules from Nuclear Magnetic Resonance Measurements of Intramolecular ^{1}H-^{1}H Proximities in Solution", *Bulletin of Mathematical Biology*, Vol. 46, No. 4, 673-698, (1984).

16) Braun, "Distance geometry and related methods for protein structure determination from NMR data", *Quarterly Review of Biophysics*, Vol. 19, 3/4, 115-157, (1987).

17) Weber, "Determining Stereo-specific ^{1}H Nuclear Magnetic Resonance Assignments from Distance Geometry Calculations", *J. Mol. Biol.*, Vol. 204, 483-487, (1988).

18) Wüthrich, "Protein Structure Determination in Solution by Nuclear Magnetic Resonance Spectroscopy", *Science*, Vol. 243, 45-50, (1989).

19) Huang, *et al.*, "Distance geometry generates native-like folds for small helical proteins using the consensus distances of predicted protein structures", *Protein Science*, Vol. 7, 1998-2003, (1998).

E.) Journal articles that describe application of distance geometry to other problems in chemistry and biology include:

20) Forster, *et al.*, "Application of distance geometry to 3D visualization of sequence relationships", *Bioinformatics Applications Note*, Vol. 15, No. 1, 89-90, (1999).

21) Newell, *et al.*, "Construction of Genetic Maps Using Distance Geometry", *Genomics*, Vol. 30, 59-70, (1995).

22) Sheridan, *et al.*, "The Ensemble Approach to Distance Geometry: Application to the Nicotinic Pharmacophore" *J. Med. Chem.*, Vol. 29, 889-906, (1986).

F.) Finally, some references to published computer programs that carry out distance geometry calculations are presented:

23) Blaney, *et al.*, "DGEOM: Distance Geometry Program", QCPE Program No. 590, *QCPE Bulletin*, Vol. 10, 37-38, (1990); Quantum Chemistry Program Exchange, Indiana University, Bloomington, IN; also, DGEOM(95), further described at: http://qcpe.chem.indiana.edu.

24) A web-based program is available at: http://iris12.colby.edu/~www/jme/dg.html and utilizes the BUILD3D program, see *e.g.*, Smith, *et al.*, "The Dendral Project: Recent Advances in Computer-Assisted Structure Elucidation," *Anal. Chim. Acta*, 1981, 133, 471–497.

25) Another web-based program is described at http://www.pasteur.fr/recherche/unites/Binfs/xplor/manual/node374.html and links therein.

These references are offered as factual support for two premises. First, that distance geometry is sufficiently well known in the art, and is susceptible to a sufficiently wide variety of applications, that one of ordinary skill in the art would be able to practice Applicant's claimed invention without being limited to the description of distance geometry found in Blaney. Second, Applicant respectfully submits that distance geometry is not "essential matter" because, as demonstrated by the volume of references in the art, it is well known in the art. As already acknowledged by the Examiner, there is "no requirement for a patent to describe what is well known in the art".

Accordingly, Applicant respectfully submits that claims 22, and 27–29, as amended herein, as well as new claims 140–143 are properly enabled according to their recited scope and kindly asks the Examiner to remove the rejection of record.

Rejections of the Claims Under 35 U.S.C. § 101

The Examiner has rejected claims 22, and 27 – 29 under 35 U.S.C. § 101 for allegedly being directed to non-statutory subject matter. Applicant respectfully traverses the rejection.

During the telephonic interview, August 20, 2004, in answer to a request from Applicant's representative to clarify the nature of the rejection, the Examiner stated that he

was issuing a "lack of statutory subject matter" rejection, and not a "lack of utility" rejection. An ensuing discussion of the Federal Circuit decision in *State Street Bank* and portions of the MPEP focused on the meaning of "useful, concrete and tangible result" and instant claim 22's production of such a result, as well as the term "physical transformation" as applied to computer-related inventions.

The Examiners collectively suggested that, if Applicant amended claim 22 to manipulate an item outside of a computer, either before or after the method steps as claimed (prior to amendment herein), then such action may bring the claim within their consideration of statutory subject matter.

Accordingly, in an effort to expedite prosecution, and to accommodate the Examiners' position, Applicant has amended claim 22 to recite a method of constructing a representation of a set of molecules stored in a computer database, thus requiring that the method act on molecular data input from some external source to the computer on which Applicant's claimed method is performed. New claim 142 recites a step of introducing the molecular data to the computer. Furthermore, a final step of claim 22 has been added by amendment herein to recite a tangible result that a representation of the molecular data has been computed. Applicant's specification shows that such a representation obviates searching every such molecule in the database when performing a query. Applicant thereby believes that claim 22 and the claims depending therefrom, as amended herein, properly recite statutory subject matter and thus are in condition for allowance.

Another alternative offered by the Examiners during the telephonic interview of August 20, 2004, was to amend claim 22 to recite a final step of comparing a test molecule with the calculated shape space. Applicant draws the Examiner's attention to claim 27, depending from claim 22, which recites a method of searching a database of molecules for molecules similar to a target molecule.

Claim 22 as amended herein, and claims depending therefrom, comply with an examination framework for computer-related inventions found on the U.S. Patent and Trademark Office website (at http://www.uspto.gov/web/offices/pac/dapp/pdf/flow.pdf), a copy of which is attached hereto as an exhibit.

Applicant now takes the Examiner through the pertinent steps of this framework. The relevant portion of the analysis begins at Box 5 ("[c]lassify the claimed invention as statutory or non-statutory"), from which the Examiner is guided to Box 6.

> At Box 6, the claimed invention is to be categorized as one of: "functional descriptive material" such as a data structure or a computer program *per se*; "non-functional

descriptive material" such as music, literary works, mere data or a computer readable medium; or a "natural phenomenon"; or none of these. Since Applicant's invention is clearly in none of these categories, the analysis proceeds to Box 8.

At Box 8, the Examiner is to consider whether the recited invention is "a Series of Steps to be performed on a computer". In the case of Applicant's invention, the answer is Yes, and the analysis moves to Box 12.

At Box 12, whether or not the invention performs Independent Physical Acts or whether it Manipulates Data representing physical objects is considered. There are two routes our of Box 12. First, the claims as amended herein *do* manipulate data (molecular fields) representing physical objects (molecules). Therefore the analysis leads to Box 14, an affirmative conclusion that Applicant's claims recite Statutory Subject Matter.

However, if it is assumed *arguendo* that Applicant's claims do not manipulate data (which they do), the ensuing analysis under such an assumption takes an alternative route which leads to Box 13.

In Box 13, an Examiner is asked to consider whether the recited invention "[m]erely manipulates an abstract idea or solves a purely mathematical problem without any limitation to a practical application." Since Applicant's claims as amended herein recite a practical application to facilitating the searching of molecular data stored on a computer, the analysis proceeds to Box 14, *i.e.*, to the conclusion that Applicant's claims recite Statutory Subject Matter.

Accordingly, under at least two ways of analyzing Applicant's recited claims according to a PTO schema, the claims are statutory subject matter.

Even if it is assumed that, were the PTO to follow through the foregoing analysis without reaching the same result, Applicant's claims remain drawn to statutory subject matter under the currently applicable law. In the response mailed March 10, 2003, Applicant discussed the standard for the patentability of mathematical algorithms set forth in *State Street Bank & Trust Co. v. Signature Financial Group, Inc.* 149 F.3d 1368 (Fed. Cir. 1998). *State Street Bank* concerned a patent for a data processing system used in the financial services industry. Whereas the most generally applicable holding of *State Street Bank* bases patentability on production of a "useful, concrete and tangible result", the Examiner has based his analysis upon a requirement of there being a 'physical transformation', a term that is not found in *State Street Bank*. Specifically, the Examiner has stated that:

> "the fact pattern of *State Street Bank* differs from the instantly pending claims which only are directed to molecular property calculations and subsequently database searching neither of which goes beyond data manipulation into a *physical transformation* or even the control of such a transformation in contrast to stock market monetary transfer."

May 19, 2004 Office Action at page 6 (emphasis added).

This distinction is without merit. First, there is nothing in the Federal Circuit's holding in *State Street Bank* to suggest that its holding should be limited to its facts (*i.e.*, manipulation of financial data). Second, the supposed 'physical transformation' of *State Street Bank* is to be found in the language of the opinion not before cited by Applicant and apparently also overlooked by the Examiner when applying the holding of the case:

> "[T]he transformation of data *** constitutes a practical application of a mathematical algorithm, formula, or calculation *** because it produces 'a useful, concrete and tangible result' – *a final share price momentarily fixed for recording and reporting purposes and even accepted and relied upon by regulatory authorities and in subsequent trades*." (emphasis added)

Thus, if the Examiner is saying that, on the one hand, the momentary fixation of a final share price in a computer system can render a claimed process useful, whereas on the other hand the momentary fixation of organized molecular property data for the purpose of facilitating searching of molecular data stored in a database does not, then Applicant respectfully disagrees with the Examiner's position.

As Applicant has previously pointed out, the organization of molecular property data is not a mere abstract exercise since "[p]harmaceutical companies maintain computer databases of all molecules they have synthesized, plus other compounds available on the market." (Specification, page 2, lines 8–9.) Furthermore, Applicant's claimed method "can be used in creating, characterizing, and searching databases of molecules based on field similarity [that] ... allow searches of a database in sublinear time." (Specification, page 10, lines 21-25.) Sublinear searching of large databases, as facilitated by Applicant's organizational scheme as recited in the instant claims, not only represents a more efficient means to search for similar molecules in large databases, it yields a tangible result that impacts the real world, namely the capacity to identify specific molecules that would otherwise have been overlooked but whose properties make them important.

Thus, it is difficult to see how such a result is any less "useful, concrete and tangible" than that of recording a share price. A share may have a paper form, and its price, although an abstract quantity, is one which may be practically manipulated by a computing machine; similarly a molecule is a physical object whose properties are abstract but which find a practical realization when stored and manipulated in numerical form on a computer.

Finally, Applicant draws the Examiner's attention to examples of recent patents, issued in 2004, that claim computer-implemented methods for manipulating data. These

patents illustrate the PTO's general recognition that such subject matter is statutory. A copy of each of these patents is attached hereto as an Exhibit.

6,725,210 ("Process database entries to provide predictions of future data values", April 20, 2004);

6,718,317 ("Methods for identifying partial periodic patterns and corresponding event subsequences in an event sequence", April 6, 2004); and

6,785,687 ("System for and method of efficient, expandable storage and retrieval of small datasets", August 31, 2004).

In each case, the first independent claim (claim 1) embodies a computer implemented method that, like Applicant's claimed method, reaches a concrete, useful, or tangible result. If the respective inventions claimed in each of these patents embodies a physical transformation then their means for so doing is indistinguishable from Applicant's. On the other hand, if such claims do not embody a physical transformation then it is clear that the requirement for a physical transformation *per se* is not sacrosanct.

In summary, Applicants respectfully submit that the instant claims embody statutory subject matter and respectfully request that the rejection of record be withdrawn.

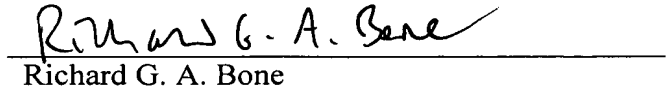
CONCLUSION

In view of the remarks presented hereinabove, Applicant respectfully submits that the subject application is in good and proper order for allowance. Withdrawal of the Examiner's rejections and early notification to this effect are earnestly solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 843-4000.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Morgan, Lewis & Bockius LLP Deposit Account No. 50-0310 for the appropriate amount. A copy of this sheet is attached.

Respectfully submitted,

Date: September 20, 2004



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Limited Recognition under 37 C.F.R. § 10.9(b)
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Appendix to
Amendment Accompanying RCE, mailed September 20, 2004
Application Serial No. 09/644,937
Attorney Docket No. 61191-0003-US

EXAMINATION PROCEDURES FOR COMPUTER-RELATED INVENTIONS

JPE JC99 SEP 2 0 2004 PATENT & TRADEMARK OFFICE